

On Certain 7-Nitro-4-Quinazolones

DISSERTATION

SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIRE-
MENTS FOR THE DEGREE OF DOCTOR OF PHILOSO-
PHY IN THE FACULTY OF PURE SCIENCE
OF COLUMBIA UNIVERSITY

BY

WILLIAM KLABER, A.B.

NEW YORK CITY

1907

EASTON, PA. :
ESCHENBACH PRINTING COMPANY.
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ACKNOWLEDGMENT.

This work was undertaken at the suggestion of Professor Marston T. Bogert and carried out under his direction. The author takes this opportunity to thank him for his valuable suggestions and advice, his encouragement, and his interest throughout the course of this research.

W. K.

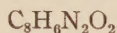
ORGANIC CHEMICAL LABORATORY,
HAVEMEYER HALL, COLUMBIA UNIVERSITY
MAY, 1907.

On Certain 7-Nitro-4-Quinazolones.

HISTORICAL INTRODUCTION.

The quinazolines, or benzomiazines, present the possibility of four isomeric *bz*-mononitro derivatives, all of which have been synthesized in the 2-methyl-4-quinazolone group.

Griess,¹ in 1869, obtained the ethyl ether of an acid,



by passing cyanogen gas into a saturated alcoholic solution of anthranilic acid; he obtained the acid itself and nitrated it. It was proved later that his acid was benzoylene urea, but the position of the nitro group in the derivative which he obtained has never been determined. In 1890, Dehoff² nitrated the anhydroacetylorthoaminobenzamide of Weddige³ (2-methyl-4-quinazolone) and obtained thereby a mononitro derivative. By the action of methyl iodide upon its potassium salt and by direct nitration of the 2,3-dimethyl-4-quinazolone the corresponding 2,3-dimethylquinazolone was prepared. The position of the nitro group in these compounds remained unproved until in 1891 Thieme⁴ obtained the same products by the action of ammonia and methyl amine on 5-nitroacetanthranilic ester. This showed Dehoff's compounds to be 6-nitroquinazolones.

In his work upon 3-nitroanthranilic ester, Zacharias⁵ synthesized 8-nitroquinazolones by the action of ammonia and primary amines upon 3-nitroacetanthranilic ester and 3-nitrobenzoylanthranilic ester. In 1896 Kratz⁶ obtained a 6-nitro-3-amino-4-quinazolone by the action of glacial formic acid on 5-nitroanthranilic hydrazide.

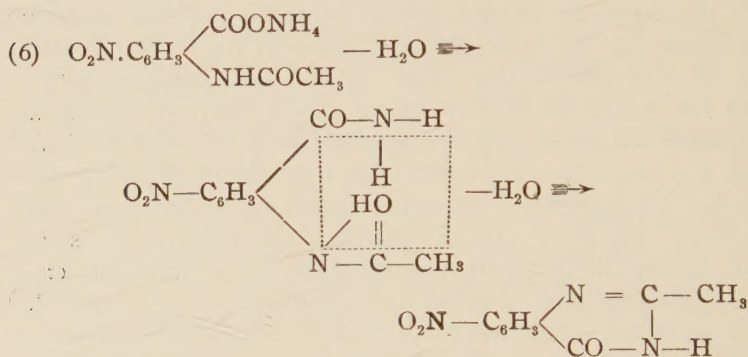
The contributions from the Havemeyer laboratories of Columbia University include the syntheses of the 5-nitro, 6-nitro, and 7-nitroquinazolones from 6-nitro, 5-nitro, and 4-nitroacetanthranils, respectively. They were prepared by the reaction of Anschütz, Schmidt, and Greiffenberg⁷ between

acetylanthranil and primary amines. The work on the 5-nitro derivatives was carried on by Bogert and Chambers⁸ and Bogert and Seil,⁹ on the 6-nitro compounds by Bogert and Cook,¹⁰ and on the 7-nitroquinazolones by Bogert and Steiner.¹¹

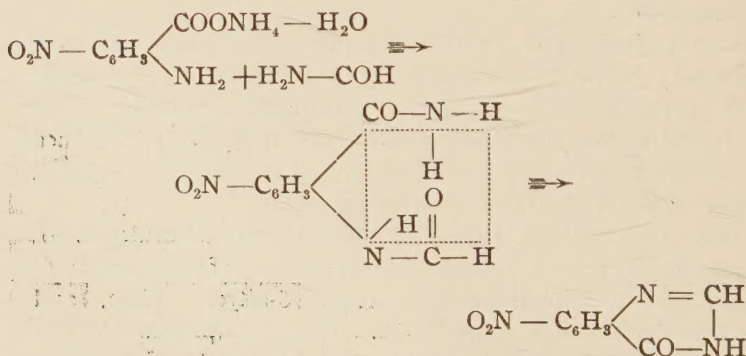
Methods of Preparation of Nitroquinazolones.

A. The 5-nitroquinazolones have been synthesized by the following methods:

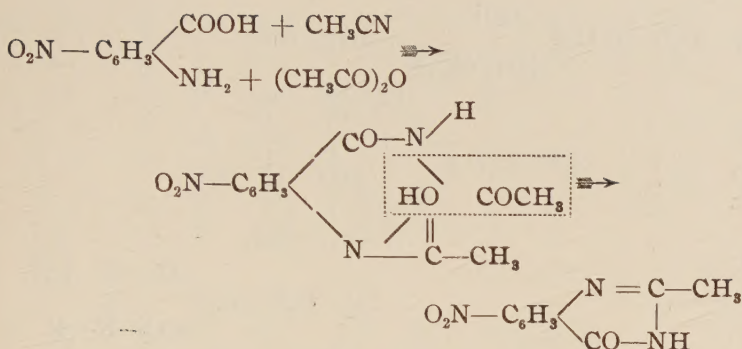
(1) By heating the ammonium salt of 6-nitroacetanthranilic acid.^{8,15}



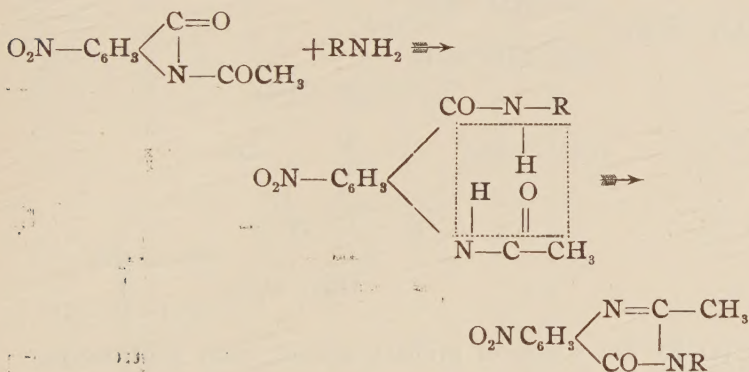
(2) By heating the ammonium salt of 6-nitroanthranilic acid with formamide.^{8,17}



(3) By heating 6-nitroanthranilic acid in sealed tubes with acetic anhydride and acetonitrile.^{8,20}

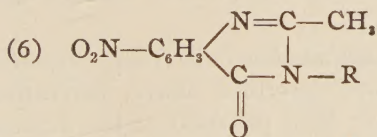
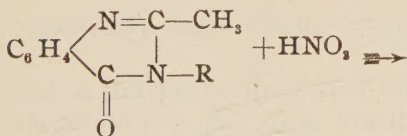


(4) By the action of primary amines upon 6-nitroacetanthranil.^{7,8,9}

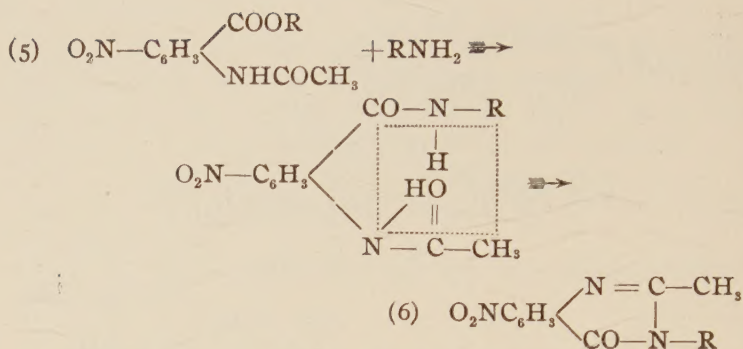


B. 6-Nitroquinazolones have been prepared by the following methods:

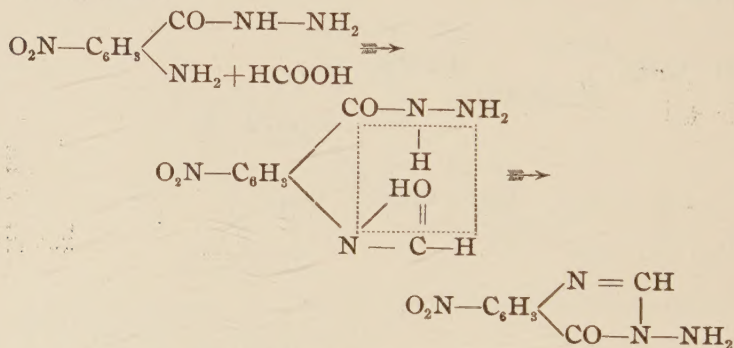
(1) By direct nitration of 2-methyl-4-quinazolones.²



(2) By the action of alcoholic ammonia and primary amines upon 5-nitroacetanthranilic ester.⁴



(3) By the action of glacial formic acid upon 5-nitroanthranilic hydrazide.⁶



(4) By the action of primary amines upon 5-nitroacetan-
thranil.^{10,7}

C. 7-Nitroquinazolones have been prepared:

(1) By fusing the ammonium salt of 4-nitroacetan-
thranilic acid.^{11,15}

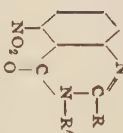
(2) By the action of primary amines upon 4-nitroacet-
anthranil.^{11,7}

D. 8-Nitroquinazolones have been prepared by the action
of alcoholic ammonia and primary amines upon 3-nitroacetyl-
anthranilic ester.⁵

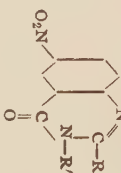
Nitroquinazolones and Their Properties.

By the methods described above, derivatives of all four
nitro isomers have been prepared in the 4-quinazolone series.
In the tables here appended are listed all nitroquinazolones
and their derivatives, prepared previous to this work, with
the exception of Griess' nitrobenzoylene urea, in which the
position of the nitro group is unknown.

5-Nitroquinazolones



6-Nitroquinazolones



7-Nitroquinazolones



8-Nitroquinazolones

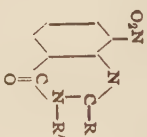


Table 1.

R=H—R'=H
White—m. p. 255°–6°
Soluble in alkalis

R=CH₃ R'=H
White—m. p. 277°–9°
Soluble in alkalis
Forms hydrochloride

R=CH₃ R'=CH₃
White—m. p. 203°

R=CH₃ R'=C₂H₅
M. p. 208°

R=CH₃ R'=C₆H₅
M. p. 233°–4°

R=CH₃ R'=NH₂

White—m. p. 152°–3°

R=CH₃ R'=quinazolinyl (Diquinazolon yl)
M. p. 306°
Forms acetic anhydride addition product

R=CH₃ R'=H
Yellow—m. p. 278°–81°
Soluble in alkalis
Forms no hydrochloride

R=CH₃ R'=CH₃
White—m. p. 165°

R=CH₃ R'=C₂H₅
M. p. 166°

R=CH₃ R'=C₆H₅
Yellow—m. p. 219°–220°

R=CH₃ R'=NH₂

White—m. p. 208°–9°

R=CH₃ R'=quinazolinyl (Diquinazolon yl)
M. p. 281°–6°

R=CH₃ R'=H
White—m. p. 290°
Soluble in alkalis
Forms hydrochloride

R=CH₃ R'=CH₃
Yellow—m. p. 151°–2°

R=CH₃ R'=C₂H₅
Yellow—m. p. 175°

R=CH₃ R'=C₆H₁₁ (i)
White—m. p. 117°–8°

R=CH₃ R'=NH—CO—NH₂

White—m. p. 266°
Forms diacetyl derivative

R=CH₃ 4-Ethoxyquinazoline
M. p. 105°–6°

R=CH₃ R'=H
Brownish—m. p. 264°
Soluble in alkalis
Forms hydrochloride

R=CH₃ R'=CH₃
White—m. p. 175°

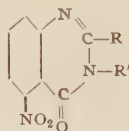
R=C₆H₅ R'=H
White—m. p. >250°

R=C₆H₅ R'=CH₃

White—m. p. 138°

In addition to the 5-nitroquinazolones listed in Table I., the following have been prepared:

Table II.



R = CH ₃ R' = C ₃ H ₇ (<i>n</i>) M. p. 204°-5°	R = C ₂ H ₅ R' = H Soluble in alkalis—m. p. 240°
R = CH ₃ R' = C ₃ H ₇ (<i>i</i>) M. p. 219°-20°	R = C ₂ H ₅ R' = CH ₃ M. p. 197°-8°
R = CH ₃ R' = C ₄ H ₉ (<i>i</i>) M. p. 202°-3°	R = C ₂ H ₅ R' = C ₂ H ₅ M. p. 181°
R = CH ₃ R' = C ₄ H ₉ (sec- ondary) M. p. 209°-10°	R = C ₂ H ₅ . 4-Methoxyquin- azoline—not obtained
R = CH ₃ R' = C ₅ H ₁₁ (<i>i</i>) M. p. 213°-14°	R = C ₂ H ₅ . 4-Ethoxyquinazo- line Unstable
R = CH ₃ R' = C ₃ H ₅ M. p. 160°-1°	R = CH ₃ R' = —N<COCH ₃ COCH ₃
R = CH ₃ . 4-Methoxyquin- azoline. Not obtained in pure condition M. p. 192°	M. p. 233° Brom derivative of above M. p. 170°
R = CH ₃ . 4-Ethoxyquinazo- line M. p. 161°	R = CH ₃ R' = NH— NHC ₆ H ₅ . Phenylhydrazone M. p. 124°-5°

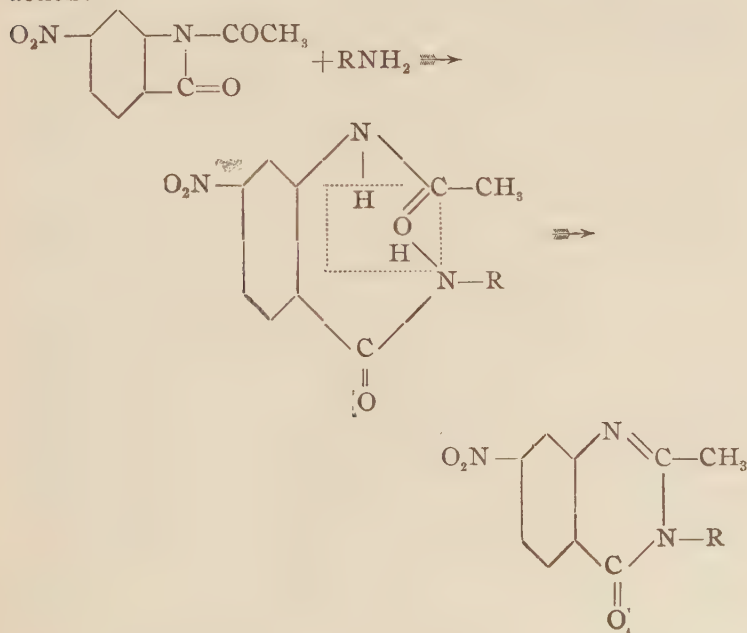
The nitroquinazolones are, in general, white or yellow crystalline solids. As regards solubility, most are easily soluble in alcohol, less so in water. They are more strongly acid than the unsubstituted compounds, exhibiting this in two ways: First, in that the hydrochlorides do not form as readily as in the unsubstituted series, requiring usually the reaction of

gaseous hydrochloric acid upon their non-aqueous solution for their formation. The hydrochlorides hydrolyze easily, yielding the free base. Second, in that the 3-hydrogen compounds, which, owing to the enol-ketonic tautomerism of the —CO—NH— group, are naturally soluble in caustic alkalies, are also dissolved by aqueous solutions of alkaline carbonates, and by concentrated aqueous ammonia. The salts of the compounds with the heavy metals form readily; the ammonium salts exist in solution only.

There seems to exist no regularity in the melting points of corresponding members of the different series of nitroisomers. In each series the 3-hydrogen compounds (*i. e.*, $\text{R}' = \text{H}$) melt much higher than their higher homologues, and it may be said, in general, that the nitroquinazolones melt higher than the corresponding unsubstituted derivatives.

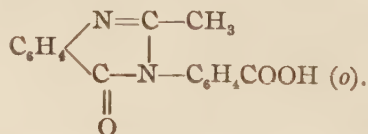
INTRODUCTION.

Bogert and Steiner¹¹ have shown that 4-nitroacetantranil condenses with primary amines with the formation of substituted nitroacetantranilamides, and that these lose water to form the 7-nitro-2-methyl-4-quinazolones according to the reaction:



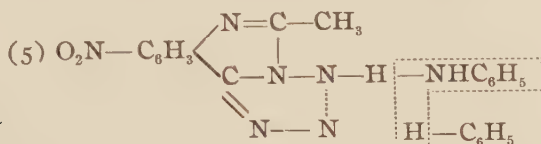
This work is a continuation of the syntheses of Bogert and Steiner,¹¹ as well as a study of the properties of their products and those synthesized by the author. All classes of amines have been used, and condensation products obtained in each case, except with amino acids. The reagents used include simple aliphatic and aromatic amines and amino derivatives, amino nitriles and esters, amino ethers and diamines, demonstrating the generality of the reaction shown above.

Preliminary work was employed in completing the series of homologues begun by Bogert and Steiner.¹¹ The solubility of the 7-nitro-2-methyl-4-quinazolone in carbonated alkalis made it necessary to determine whether this action was due to the acidic influence of the nitro group. It was accordingly reduced to the corresponding amino derivative, which is insoluble in carbonated alkalis. The work on amino acids, nitriles and esters was undertaken with two objects in view. The weakly basic properties of the free acids made it of interest to determine whether condensation would take place with 4-nitroacetanthranil. One such compound has been reported by Anschütz, Schmidt, and Greiffenberg,¹⁸ who, in addition to acetanthranil, obtained by the action of phosphorus oxychloride on acetanthranilic acid an orthoquinazolonylbenzoic acid of the formula



In this work no condensation was observed between amino acids and nitroacetanthranil. The possibility of elimination of one molecule of water between acid amide groups in the "3" position and the keto group at "4" presented the second object. Bogert and Seil⁹ found that the 7-nitro-3-uraminoquinazolone did not follow this course when treated with dehydrating agents, but formed an acetyl derivative with acetic anhydride. Both the quinazolonylacetamide and quinazolonylbenzamide, when treated with acetic anhydride, were dehydrated with the formation of the corresponding nitriles.

The 3-aminoquinazalone and diquinazolonyl were synthesized, paralleling the work of Bogert and Seil⁹ and Bogert and Cook.¹⁰ From the former were obtained a mono- and a diacetyl derivative. Various recent articles¹⁹ have shown that primary amino groups attached to nitrogen possess the property of condensing with diacetosuccinic diethyl ester to form pyrrol derivatives. The aminoquinazalone undergoes this reaction, yielding a quinazolonyl pyrrol derivative. With the 5-nitro-3-aminoquinazalone, Bogert and Seil⁹ obtained, by the action of phenylhydrazine the phenylhydrazone of the 3-phenylhydrazinoquinazalone. Such a compound should yield, by loss of one molecule of aniline, as indicated,



a new osotetrazole derivative. In the 7-nitro series, following similar conditions, no such compound, or even the intermediate product, has been obtained. The reaction produced a compound, well defined and crystalline, which has not as yet been identified.

Methods have been devised for passing from the monoacetaminoquinazalone to the diacetamino compound, and *vice versa*. Oxidation of these derivatives was attempted with the object of transforming the methyl group to a carboxyl group. Such a compound would present the possibility of dehydration to an anthranil structure and subsequent condensation of the compound thus derived with primary amines. Neutral permanganate ruptured the miazine cycle, producing nitroacetanthranilic acid.

The unsatisfactory result obtained by the action of phenylhydrazine upon the aminoquinazalone caused attention to be turned to the action of this reagent upon the monoacetaminoquinazalone. Here exists the possibility not only of the formation of a hydrazone, but of subsequent loss of water to produce a new tetrazine derivative. In alcoholic solution no reaction

took place. By direct fusion of the quinazolone with phenylhydrazine, the hydrazone was formed, but no tetrazine derivative was obtained. From this result it seems probable that one action of the phenylhydrazine upon the amino compound would be the formation of the hydrazone.

The condensations with ethylenediamine proved unsatisfactory in that the reaction produced the intermediate amides instead of the ethylene diquinazolonyl. Only a small amount of the latter compound has been obtained, the quantity being insufficient to procure all the necessary analytical data.

EXPERIMENTAL.

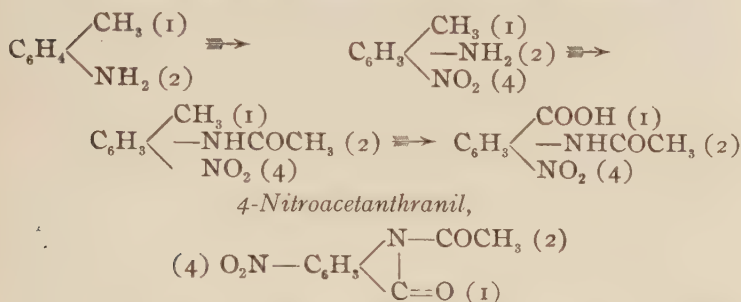
Preparation of 4-Nitroacetanthranilic Acid.

Orthotoluidine was converted into 4-nitroorthotoluidine by the method of Nölting and Collin¹³ in the presence of a large amount of concentrated sulphuric acid, keeping the temperature between 0° C. and 5° C. When the nitration was completed, the reaction mixture was diluted and neutralized with caustic soda, preventing, as well as possible, any considerable rise in temperature by the addition of ice. The crude 4-nitroorthotoluidine thus obtained in 78 per cent yield, was heated for a short time with acetic anhydride, the hot solution poured into an equal volume of alcohol and allowed to crystallize. The yield is practically theoretical.

This crude product was dried in an air bath at 80° C. and then oxidized in fifty-gram lots by potassium permanganate in the presence of magnesium sulphate.¹⁴ The most advantageous conditions were found to be as follows: For fifty grams of the nitroacetoluide, one hundred grams of magnesium sulphate, one hundred and seventeen grams of potassium permanganate in five to six liters volume of water. The solution was maintained hot on a water bath, and steam passed in to keep it in motion. When all the permanganate had been decomposed the solution was filtered hot, and the filtrate, when cooled, acidified with hydrochloric acid. Practically pure 4-nitroacetanthranilic acid was thus obtained, in yields varying between 60 per cent and 80 per cent of the theoretical, depending upon the purity of the acetoluide used. A few grams of the red 4-nitroanthranilic acid may be obtained

from the acid filtrate by concentrating and neutralizing with soda.

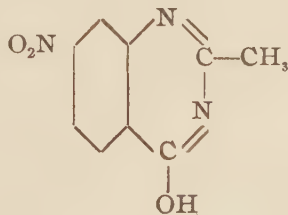
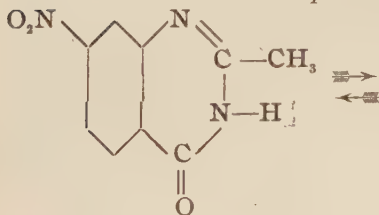
The process may be presented graphically as follows:



Dry 4-nitroacetanthranilic acid was heated with an excess of acetic anhydride, evaporated to drive off the acetic acid formed in the reaction, and allowed to cool. If the solution is allowed to cool slowly, square yellow-greenish plates of the anthranil are obtained. For the purpose of condensations with primary amines, it was found to be advantageous to cool the acetic anhydride solution under the water tap, keeping in motion. The nitroacetanthranil is then obtained in finely divided form and is practically white, m. p. $137^{\circ}\text{--}8^{\circ}$.

3-ALKYLQUINAZOLONES FROM 4-NITROACETANTHRANIL.

7-Nitro-2-methyl-4-quinazolone (7-Nitro-2-methyl-4-oxyquinazoline).



This compound was first prepared by Bogert and Steiner.¹¹ It was prepared by two methods in this work:

I. 4-Nitroacetanthranilic acid was treated with an excess of ammonia water,¹⁵ evaporated to dryness and then fused in an oil bath at 225° C. The cold melt was pulverized, washed with water, then dissolved in alcohol, bone-blackened, and allowed to crystallize.

II. 4-Nitroacetanthranil was added with stirring to concentrated aqueous ammonia, heated for a short time, diluted with water and a little diluted caustic potash solution. This was then boiled until the conversion to the quinazalone from the acetanthranilamide was practically complete. The cooled solution was filtered, the product dissolved in dilute caustic potash, and carbon dioxide passed into the solution until the precipitation was complete. The precipitate was crystallized from alcohol.

The products obtained by the two methods are identical, m. p. 290° C. (corr.). Pale greenish, silky needles. This quinazalone, on account of its enolic-ketonic tautomerism, is soluble in caustic alkalies. The acid influence of the nitro group causes it to be soluble in alkali carbonates, but not bicarbonates, and in concentrated aqueous ammonia. From the latter solvent it is reprecipitated on boiling out the excess of ammonia. It is not affected by long fusion with ammonium acetate.

Potassium Salt.—7-Nitro-2-methyl-4-quinazalone was dissolved in dilute potassium hydroxide and the solution saturated with solid potassium carbonate. The potassium salt separated as a bright yellow precipitate. This was filtered and dried, then extracted with absolute alcohol and evaporated to dryness. It crystallizes with alcohol on crystallization, but loses part of this on standing in the air. Dried to constant weight, it turns dark yellow.

0.5082 gram of air-dried substance lost 0.0640 gram when dried to constant weight = 12.79 per cent. The dry salt, titrated with $N/5$ H_2SO_4 , phenolphthalein as indicator, used 9.2 cc.

K—Found—16.21 per cent. Theoretical for $C_9H_6N_3O_3K = 16.11$ per cent.

Silver Salt.—The 7-nitro-2-methyl-4-quinazalone was dissolved in concentrated aqueous ammonia and heated to boiling. The silver salt was precipitated by adding ammoniacal silver nitrate solution. The voluminous yellow precipitate was washed well with dilute ammonia water and then dried. It is slowly but quantitatively decomposed by heating with a salt solution. It was analyzed by this method, titrating the sodium salt formed with standard sulphuric acid.

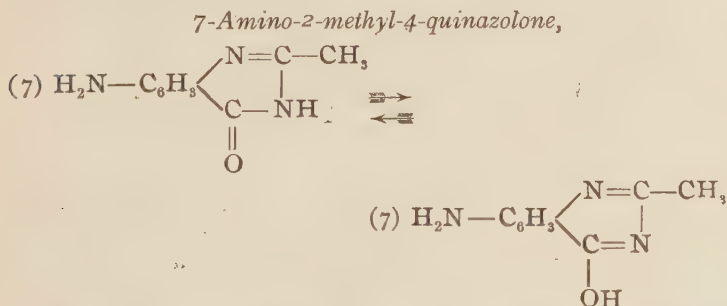
0.5028 gram used 8 cc. $N/5 H_2SO_4$.

Ag—Found—34.35 per cent. Theoretical for $C_9H_6N_3O_3Ag = 34.60$ per cent.

Oxidation of the 2-methyl-4-quinazalone was attempted by dissolving it in 1:5 sulphuric acid containing chromic anhydride. The solution was boiled during the daytime for one and one-half weeks. At the end of a week there had crystallized out of the cold solution small white needle crystals, which melted sharply at $327^\circ C.$ (uncorr.). They were soluble in caustic and carbonated alkalis, producing a red color; soluble in alcohol, crystallizing in small needles. Only a small amount of this product was obtained, and it has not been identified.

Analysis for nitrogen showed 20.48 per cent and 20.63 per cent. Carbon, 47.36 per cent; hydrogen, 3.42 per cent.

The 7-nitro-2-methyl-4-quinazalone is reduced very readily by stannous chloride to the



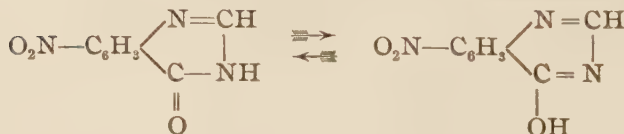
Fifty per cent excess of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ over the theoretical

amount was dissolved in concentrated hydrochloric acid and heated. To the hot solution the 7-nitroquinazolone was added gradually, with shaking. When all had been added the solution was boiled for half an hour and then allowed to cool. A double tin chloride of the desired compound crystallized out and was filtered. The precipitate was treated with a dilute solution of carbonate, filtered hot from the precipitated hydrated tin oxide and cooled. Long, white, silky needles were obtained and subsequently crystallized from a small amount of alcohol. The concentrated hydrochloric acid solution remaining after the separation of the quinazolone contained practically none of the desired product.

The 7-aminoquinazolone corresponds exactly in its properties with that obtained simultaneously by Bogert and Chambers¹⁶ by the action of ammonia on 4-acetaminoacetantranil. It is soluble in hot water and alcohol, crystallizing from them with one-half molecule of water or alcohol of crystallization, respectively; soluble in caustic alkalies, but in contrast with the corresponding nitro derivative, it is not soluble in carbonates. It gives an isonitrile test of not unpleasant odor. M. p. $311^{\circ}\text{C. (corr.)}$.

0.1720 gram, as crystallized from alcohol, lost, on drying to constant weight at 110°C. , 0.0209 gram = 12.15 per cent. One-half mol. of $\text{C}_2\text{H}_5\text{OH}$ of crystallization. Theoretical = 11.62 per cent. N on dried sample, 24.22 per cent. Theoretical for $\text{C}_9\text{H}_9\text{N}_3\text{O}_3$ = 24.00 per cent.

7-Nitro-4-quinazolone (7-Nitro-4-oxyquinazoline).

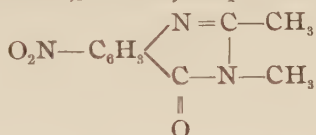


This was prepared by Niementowski's¹⁷ reaction from 4-nitroanthranilic acid and formamide. The 4-nitroanthranilic acid was obtained by dissolving 4-nitroacetantranilic acid in alcohol, adding 5 cc. concentrated sulphuric acid, and boiling for a short time. The solution was then poured into a large volume of water, causing the precipitation of the desired prod-

uct. It was filtered and then fused with an excess of formamide. On cooling, the residue was dissolved and bone-blackened in alcohol and allowed to crystallize. Long, slender, yellow needle crystals were obtained, soluble in caustic alkalies. M. p. 276°C . (corr.).

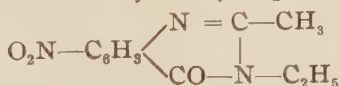
N—Theoretical for $\text{C}_8\text{H}_5\text{N}_3\text{O}_3 = 22.00$ per cent. Found, 22.21 per cent.

7-Nitro-2,3-dimethyl-4-quinazolone,



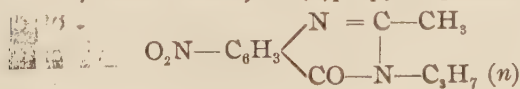
This was previously prepared by Bogert and Steiner¹¹ from 4-nitroacetanthranil and methyl amine. The identical compound was obtained by dissolving 4-nitroacetanthranilic acid in aqueous methyl amine, evaporating to dryness and fusing in an oil bath at 160°C . The cold melt was extracted with alcohol and bone-blackened. The yield is poor. M. p. $151^{\circ}-2^{\circ}\text{C}$. (corr.). The quinazolone is unaffected by boiling ammonium acetate.

7-Nitro-2-methyl-3-ethyl-4-quinazolone,



This was previously prepared by Bogert and Seil.¹² It melts at 175°C . (corr.).

7-Nitro-2-methyl-3-(n)propyl-4-quinazolone,

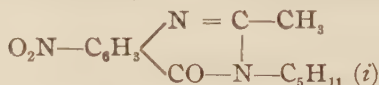


4-Nitroacetanthranil was added to dilute propyl amine and heated on a sand bath. A clear solution resulted, which on further heating formed an emulsion and then separated out as an oil. When cooled, dilute acetic acid was added to acid reaction, and the oil caused to solidify by scratching the sides of the beaker. The product was bone-blackened and crys-

tallized from dilute alcohol. Slightly greenish feathery clusters. Soluble in alcohol. M. p. 140° C. (corr.).

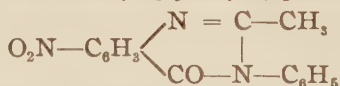
N—Theoretical for $C_{12}H_{13}N_3O_3 = 17.00$ per cent. Found, 16.89 per cent.

7-Nitro-2-methyl-3-(i)amyl-4-quinazolone,



This was previously prepared by Bogert and Seil¹² from 4-nitroacetanthranil and isoamylamine. M. p. 117°–8° C. (corr.).

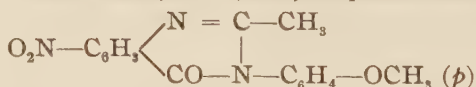
7-Nitro-2-methyl-3-phenyl-4-quinazolone,



4-Nitroacetanthranil was heated with an excess of aniline. On cooling, the quinazolone separated. The excess of aniline was removed with dilute acetic acid and the product crystallized from large quantities of alcohol. Brownish, diamond-shaped plates, soluble in alcohol. M. p. 209° C. (corr.).

N—Theoretical for $C_{15}H_{11}N_3O_3 = 14.94$ per cent. Found, 14.82 per cent.

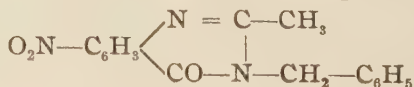
7-Nitro-2-methyl-3-(p)anisyl-4-quinazolone,



An excess of *p*-anisidine and 4-nitroacetanthranil were heated together on a sand bath. The fusion solidified after short heating, and when cooled was digested with hot dilute hydrochloric acid, filtered, and washed with hot water. The remaining quinazolone was bone-blackened and crystallized from alcohol. Square yellow plates. M. p. 228° C. (corr.).

N—Theoretical for $C_{18}H_{13}N_3O_4 = 13.50$ per cent. Found, 13.49 per cent.

7-Nitro-2-methyl-3-benzyl-4-quinazolone,



4-Nitroacetanthranil was heated with an excess of diluted benzylamine. A red oil separated, which solidified on cooling. The reaction product was treated with hydrochloric acid, filtered and bone-blackened in alcoholic solution. Two products were separated by fractional crystallization:

1. Compact yellow crystals, melting at 221° C. (uncorr.). On further purification by recrystallization from alcohol, this compound changed completely to the 3-benzylquinazolone. It was shown later that this was the hydrochloride of the latter.

2. The 3-benzylquinazolone, which crystallized in small yellow cubes. It is readily soluble in alcohol. M. p. $131^{\circ}-2^{\circ}$ C. (corr.).

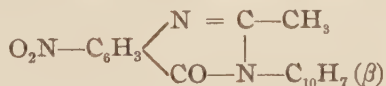
N—Theoretical for $C_{16}N_{13}N_3O_3 = 14.23$ per cent. Found, 14.27 per cent.

Hydrochloride.—This was prepared in order to identify the compound obtained in the original condensation, which melted at 221° C. (uncorr.). Pure 3-benzylquinazolone was dissolved in hot ethyl acetate and a stream of dry hydrochloric acid gas passed into the boiling solution. The hydrochloride precipitated immediately in compact yellow crystals. M. p. 223° C. (uncorr.) $229^{\circ}-30^{\circ}$ C. (corr.).

N—Theoretical for $C_{16}H_{14}N_3O_3Cl = 12.67$ per cent. Found, 12.92 per cent.

It is identical with the compound obtained before, hydrolyzing on boiling for a short time in alcohol solution.

7-Nitro-2-methyl-3-(β)naphthyl-4-quinazolone,



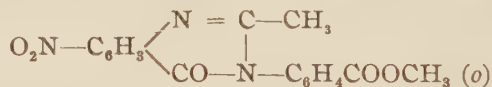
This was obtained by direct fusion of an excess of β -naphthylamine with 4-nitroacetanthranil. After short heating, the melt solidified; it was then extracted with hot dilute hydrochloric acid, filtered and washed with hot water. The product remaining was bone-blackened and crystallized from alcohol. Clusters of feathery white needles resulted, soluble in large quantities of alcohol. M. p. $218^{\circ}-19^{\circ}$ C. (corr.).

N—Theoretical for $C_{19}H_{13}H_3O_3 = 12.68$ per cent. Found, 12.64 per cent.

CONDENSATIONS WITH AMINO ESTERS AND AMINO NITRILES.

In this work, the attempts to condense glycooll and anthranilic acid with 4-nitroacetantranil were unsuccessful. Water solutions of the free acids and their sodium salts hydrolyzed the anthranil on heating; direct fusion of the two reagents caused decomposition with both acids. Amino esters and amino nitriles were tried and the corresponding quinazolones obtained. The ease of reaction of nitriles with derivatives of anthranilic acid made it necessary to determine whether nitriles would condense with 4-nitroacetantranil. To this end the anthranil was heated with dry acetonitrile and benzonitrile. In neither case did any reaction take place under atmospheric pressure. Acetonitrile was also tried in a sealed tube at $160^\circ C.$, but here also the unchanged acetantranil was recovered.

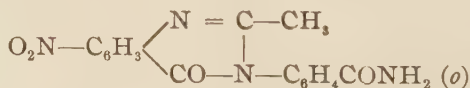
7-Nitro-2-methyl-4-quinazolonyl-3-orthobenzoic methyl ester.



Anthranilic methyl ester in excess of the theoretical quantity was added to 4-nitroacetantranil and heated for a short time. The resulting melt was allowed to cool, then dissolved, bone-blackened and crystallized from alcohol. The product thus obtained was treated in the cold with dilute potassium hydrate to extract any nitroacetantranilic acid, and the residue recrystallized from alcohol. Minute, bright yellow, granular crystals were obtained. M. p. $175^\circ C.$ (corr.); insoluble in water, soluble in alcohol.

N—Theoretical for $C_{17}H_{13}N_3O_5 = 12.38$ per cent. Found, 12.52 per cent.

7-Nitro-2-methyl-4-quinazolonyl-3-orthobenzamide.



This compound was obtained by condensing 4-nitroacetan-

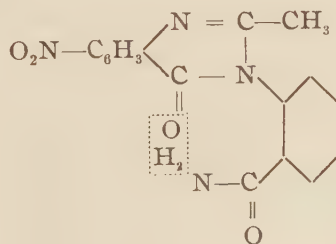
thranil with anthranilic nitrile in the presence of water. The saponification of the nitrile group is noteworthy, as anthranilic nitrile saponifies with difficulty.

Anthranilic nitrile in calculated quantity was just covered with water and heated to boiling. To the boiling solution, in which the nitrile remained as a yellow oil, 4-nitroacetanthranil was added, immediate condensation taking place. The oily nitrile became dark and solidified; finally a precipitate formed from the supernatant liquid. On cooling, potassium carbonate was added to dissolve the nitroacetanthranilic acid which had separated, the solution filtered and the residue extracted with ethyl acetate, which removed the colored by-product of the reaction. The compound remaining was crystallized from nitrobenzol, and the solvent removed by washing with cold alcohol. Straw-colored needle crystals resulted, soluble in nitrobenzol, acetic anhydride and large quantities of alcohol. M. p. $320^{\circ}-1^{\circ}$ C. (corr.).

N—Theoretical for $C_{16}H_{12}N_4O_4 = 17.30$ per cent. Found, 17.31 per cent, 17.34 per cent, 17.28 per cent.

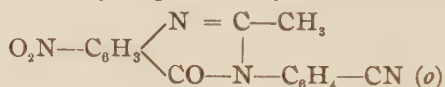
This compound is isomeric with 4-nitro-2-acetoamino, benzoyl anthranilic nitrile. That it is not the latter is shown by the fact that it is unchanged on long boiling in nitrobenzol solution. The substituted benzoylanthranilic nitrile is the intermediate product in the formation of the quinazolonyl benzonitrile (see below) and does condense to that compound in nitrobenzol solution.

By the elimination of a molecule of water between the keto group of the quinazolone and the two hydrogens of the amide group, a new heterocycle would be formed in the following manner:



With this end in view, the quinazolonyl benzamide was boiled for two hours in just sufficient acetic anhydride to dissolve it. On cooling, the product crystallizing was found to be the quinazolonyl benzonitrile.

7-Nitro-2-methyl-4-quinazolonyl-3-orthobenzonitrile.

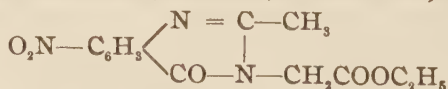


By the direct fusion of anthranilic nitrile with 4-nitroacet-anthranil, unsatisfactory results were obtained. In one case the ether extract of the fusion product yielded reddish needles in small quantities, which were identical with the quinazolonylbenzonitrile formed in nitrobenzol solution.

The method of obtaining the desired product consisted of dissolving the calculated quantity of anthranilic nitrile in about 30 cc. of nitrobenzol, heating to boiling and then adding 4-nitroacetanthranil. After boiling for thirty minutes (long boiling is essential), the solution was allowed to cool; a red product crystallized, which, after filtration, was purified by dissolving and bone-blackening in benzol, evaporating the solvent and crystallizing from alcohol. Care must be taken in dissolving in alcohol, not to boil for any length of time, since this causes the saponification of the nitrile group to the quinazolonylbenzamide. The compound, purified in the above manner, crystallizes in slender, yellow needle crystals, with a reddish tinge; soluble in benzol, ether, alcohol, acetic anhydride and nitrobenzol. M. p. 234°C . (corr.).

N—Theoretical for $\text{C}_{16}\text{H}_{10}\text{N}_4\text{O}_3 = 18.30$ per cent. Found, 18.45 per cent, 18.23 per cent.

7-Nitro-2-methyl-4-quinazolonyl-3-acetic Ethyl Ester,

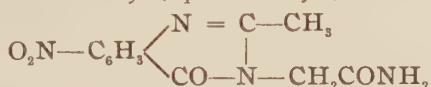


Three and five-tenths grams of glycine ethyl ester hydrochloride were dissolved in a small quantity of cold water and the free ester liberated by adding the moist silver oxide from 4.66 grams of silver nitrate. To the solution containing the

precipitated silver chloride 5 grams of 4-nitroacetantranil were added and the mixture heated to boiling on a sand bath. After short boiling, the solution became clear, followed by the appearance of turbidity. When cooled, the bulk of the reaction product remained as a sticky mass, mixed with the silver chloride. The liquor was decanted and extracted with ether. The reaction product was extracted with large quantities of ether and by repeated crystallization from this solvent, the quinazolone was obtained in white, sheaf-like crystals, melting at $139^{\circ}\text{--}40^{\circ}\text{C}$. (corr.).

N—Theoretical for $\text{C}_{13}\text{H}_{13}\text{N}_3\text{O}_5 = 14.43$ per cent. Found, 14.38 per cent.

7-Nitro-2-methyl-4-quinazolonyl-3-acetamide,



This compound was prepared by boiling the quinazolonyl acetic ester with concentrated aqueous ammonia. The resulting product was crystallized from alcohol. White feather crystals. M. p. 275°C . (corr.).

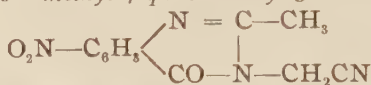
N—Theoretical for $\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}_4 = 21.37$ per cent. Found, 21.45 per cent.

In order to determine whether this quinazolonyl amide would dehydrate to the corresponding nitrile, as was found with the quinazolonyl benzamide, it was boiled for four hours in sufficient acetic anhydride to dissolve it. The solvent was then evaporated to as small a bulk as possible and the remainder decomposed by boiling with water. The reaction product, which separated, was dissolved and bone-blackened in acetone, the latter evaporated, and the residue crystallized from dilute acetic acid. Very thin white plates were thus obtained, which melted at $202^{\circ}\text{--}3^{\circ}\text{C}$. Analysis showed 22.36 per cent N. A melting point of a mixture of this compound and the quinazolonylacetone nitrile showed practically no depression from that of the latter. The nitrile, crystallized in the same manner, showed the same crystalline form. From these considerations the two compounds were proved to be identical,

the difference in melting points and the lowness of the analytical result being due probably to some slight impurity.

From the mother liquors of the above crystallization, on concentrating and nearly neutralizing with caustic potash, a flocculent purple precipitate was obtained. It was not investigated further.

7-Nitro-2-methyl-4-quinazolonyl-3-acetonitrile,

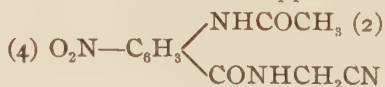


Four and seventeen hundredths grams of potassium hydroxide were dissolved in a small amount of water and, after cooling the solution, 5.7 grams of aminoacetonitrile sulphate were added slowly to prevent any considerable rise in temperature. When all had been added, 5 grams of 4-nitro-acetantranil were added and the whole heated quickly to boiling. The heating was continued for five minutes, during which time the solution had become dark red. The cooled solution was diluted with water, filtered, and the product obtained dissolved and bone-blackened in acetone, evaporated to small bulk and crystallized. Yellow rhomboidal plates separated, which, after one further crystallization, melted sharply at $207^{\circ}-8^{\circ}$ C. (corr.). Easily soluble in acetone, alcohol, dilute acetic acid; insoluble in water.

N—Theoretical for $\text{C}_{11}\text{H}_8\text{N}_4\text{O}_3 = 22.90$ per cent. Found, 23.10 per cent.

The acetone mother liquor remaining after the separation of the quinazolone contained the intermediate reaction product.

4-Nitro-2-acetaminohippuronitrile,



To obtain this product in pure condition the acetone solution was evaporated further, diluted carefully with gasoline, ligroin, or benzine, until just turbid, and the turbidity removed by the addition of a few drops of acetone. By this means it was hoped to remove all the quinazolone, which is

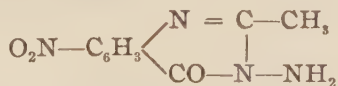
the more insoluble of the two, and to leave the substituted hippuronitrile in solution. The resulting crystals were filtered and the mother liquor diluted largely with gasoline, causing the precipitation of the solute. This was again dissolved in acetone, diluted carefully as before, but no matter how often the fractional separation was carried out, the prism crystals of the hippuronitrile were always found to be contaminated with the rhomboidal plates of the quinazolone, if the crystallization were allowed to proceed slowly. In view of the fact that the more soluble amide always appeared first and the plates only on long standing, it seems probable that the former, on standing in this solution, loses water and forms the quinazolone. The substituted hippuronitrile was obtained in pure condition either by picking out the prisms from the plates or by precipitating by the addition of a large volume of gasoline after carrying out the fractional crystallization once. By the former method a purer product was obtained; by the latter, very fine, almost white, needles. M. p. 194°C . (corr.), with effervescence. They are very soluble in acetone, and on boiling with very dilute caustic potash change to the quinazolone, accompanied with much decomposition.

N—Theoretical for $\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}_4 = 21.37$ per cent. Found, 21.53 per cent.

When 4-nitroacetantranil was fused with β -aminocrotonic ester, after short heating, the fusion solidified. The product was extracted with alcohol and purified by recrystallization. It proved to be the 7-nitro-2-methyl-4-quinazolone, m. p. 290°C . (corr.). The heating evidently caused the β -amino ester to decompose with the formation of ammonia; this then condensed with 4-nitroacetantranil.

CONDENSATIONS WITH HYDRAZINE.

7-Nitro-2-methyl-3-amino-4-quinazolone,



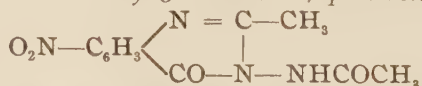
This was obtained from hydrazine hydrate and hydrazine sulphate with 4-nitroacetantranil by two slightly different methods.

From hydrazine hydrate: 4-nitroacetantranil was added gradually to an excess of 50 per cent hydrazine hydrate. Reaction took place immediately, the solution turning red; upon further addition, the reaction proceeded with evolution of heat. The reaction product was heated for a short time, then allowed to cool and extracted with a small amount of alcohol to remove most of the impurities. The residue was then crystallized to constant melting point from alcohol, yielding long, slender, yellow needle crystals melting at 223°C . (corr.).

N—Theoretical for $\text{C}_9\text{H}_8\text{N}_4\text{O}_3 = 25.45$ per cent. Found, 25.73 per cent, 25.74 per cent.

From hydrazine sulphate: Fifty per cent excess of hydrazine sulphate over the theoretical quantity was just covered with water and to this was added the calculated amount of solid potassium hydroxide (calculated as 100 per cent). The result was a hot concentrated solution of hydrazine containing precipitated potassium sulphate. To this hot solution the weighed amount of 4-nitroacetantranil was added in portions, stirring after each addition; the mixture was then heated on a sand bath until it had passed through a red color to a bright yellow mass. It was then allowed to cool, water added and a little dilute potassium hydroxide, boiled for five minutes, filtered hot and washed with hot water. The insoluble product was purified by bone-blackening and crystallizing from alcohol. It is identical with that obtained from the hydrate. Yield, 50 per cent of the theoretical.

7-Nitro-2-methyl-3-acetamino-4-quinazolone,



The 3-aminoquinazolone was heated with just sufficient acetic anhydride to dissolve it, evaporated nearly to dryness, and when cool, the thick syrupy residue was caused to solidify by scratching the beaker. It was filtered and the excess of acetic anhydride removed with a small amount of carbon tetrachloride. It is best purified by dissolving and bone-blackening in benzol. In this manner it can readily be separated from any diacetyl derivative which may be formed at the

same time. Short, white, heavy prisms are obtained, soluble in alcohol, benzol, and acetic anhydride; the last converts it into the diacetaminoquinazolone.

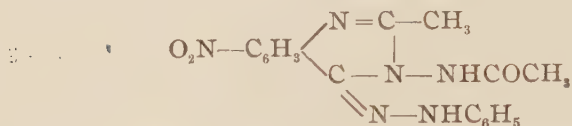
The monoacetyl derivative is also obtainable by boiling the aminoquinazolone in glacial acetic acid solution with the calculated quantity of acetic anhydride, plus the amount of the latter sufficient to convert the solvent into 100 per cent acetic acid. The solution was boiled for one hour under a reflux condenser, then evaporated nearly to dryness and treated as before. Some of the monoacetaminoquinazolone was obtained in this manner, but the yield is poor. M. p. 233°C . (corr.).

N—Theoretical for $\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}_4 = 21.37$ per cent. Found, 21.49 per cent.

The attempts made to form a phenylhydrazone of the diacetaminoquinazolone led to the discovery that the latter, when heated in alcoholic solution in the presence of an organic base, was converted into the monoacetyl derivative. Two trials were made to form the phenylhydrazone by boiling in alcoholic solution, acid with acetic acid, with the calculated amount of phenylhydrazine. The solution was boiled under a reflux condenser for two to three hours, the alcohol then evaporated, and the concentrated solution diluted with water. The precipitate was filtered and dried and extracted with a small amount of benzol. The insoluble residue consisted of practically pure monoacetaminoquinazolone. This behavior suggested that the presence of a base in the alcoholic solution might accomplish the same purpose. The diacetaminoquinazolone was therefore treated in alcoholic solution with an excess of aniline, boiled for two hours, the greater part of the solvent evaporated, and the remainder treated as before. Again the monoacetyl derivative was obtained.

In view of these results, direct fusion of the monoacetaminoquinazolone with phenylhydrazine was tried, with the production of the

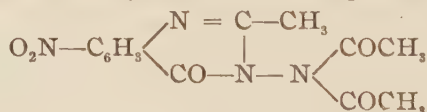
Phenylhydrazone of 7-Nitro-2-methyl-3-acetamino-4-quinazoline,



The 3-acetaminoquinazoline was just covered with phenylhydrazine, and the mixture heated on a sand bath. When heated to boiling the flame was removed and the reaction allowed to complete itself. If large quantities are used the reaction proceeds with great violence and much frothing, finally solidifying. With smaller quantities, or too much phenylhydrazine, after the cessation of the reaction, the fusion is again heated and most of the phenylhydrazine removed in this way; on cooling, the melt solidified. It was then washed with ether and the residue crystallized from alcohol. Pale yellow prisms were obtained, melting at 315°C . (corr.).

Theoretical for $\text{C}_{17}\text{H}_{16}\text{N}_6\text{O}_3 = \text{N}$ 23.86 per cent; C, 57.95 per cent; H, 4.54 per cent. Found = N, 23.4 per cent; C, 57.60 per cent; H, 4.90 per cent.

7-Nitro-2-methyl-3-diacetamino-4-quinazoline,



This compound may be obtained in two ways: (1) By treating the 3-aminoquinazoline with a large excess of acetic anhydride, or (2) by retreating the monoacetyl derivative with acetic anhydride. In both cases the solution so obtained was evaporated to very low bulk and, after cooling, the product caused to crystallize by scratching the beaker. This was filtered, washed with carbon tetrachloride and bone-blackened in benzol solution. The excess of benzol was evaporated and gasoline added until the solution became turbid. It was then warmed till clear and allowed to crystallize. Light yellow, oblong plates were obtained, easily soluble in benzol, alcohol and acetic anhydride. When boiled in alcoholic

solution in the presence of an organic base, it is changed to the monoacetyl derivative. M. p. 132° C. (corr.).

N—Theoretical for $C_{13}H_{12}N_4O_5 = 18.42$ per cent. Found, 18.79 per cent, 18.89 per cent.

Oxidation of this compound with neutral potassium permanganate ruptured the miazine cycle, producing thus 4-nitroacetanthranilic acid. Five grams of the diacetaminoquinazolone were treated with a solution of 9 grams of potassium permanganate and 10 grams of magnesium sulphate. The solution was heated on a boiling water bath; all the permanganate reduced very quickly and the hydrated manganese dioxide was filtered. The clear solution was concentrated, and when acidified, yielded a mixture of 4-nitroacetanthranilic acid and 4-nitroanthranilic acid. Other oxidizing agents have not been tried.

Action of Phenylhydrazine on the 3-Aminoquinazolone.

As has been stated previously, Bogert and Seil⁹ prepared the phenylhydrazone of the 5-nitro-2-methyl-3-phenylhydrazino-4-quinazolone. They obtained this derivative in two ways: (1) By direct fusion with phenylhydrazine of the 5-nitro-3-aminoquinazolone. (2) By boiling the aminoquinazolone with phenylhydrazine in alcoholic solution, slightly acid with acetic acid. In the 7-nitro series the reaction has been carried out as follows:

I. 7-Nitro-2-methyl-3-amino-4-quinazolone was heated in a small beaker with an excess of phenylhydrazine. When just heated to boiling, the flame was removed and the reaction allowed to complete itself. Ammonia was evolved. At the close of this reaction the fusion product was again heated for a short time, then allowed to cool somewhat, and acidified with glacial acetic acid. When heated again, a vigorous reaction, accompanied by deep coloration, took place, which was later proved to be due, at least in part, to the formation of acetphenylhydrazide. At the close of the reaction, the product was allowed to crystallize, then filtered and washed with ether until pure white. It was then dissolved in water just alkaline with caustic potash and crystallized in long, fine needle crystals, which were subsequently purified by crystal-

lization from alcohol. The product was white, feathery clusters, melting sharply at 230° C. (uncorr.), easily soluble in hot water, in alcohol but insoluble in ether.

Analyses for C, H, and N gave the following results:

C, 48.82 per cent; H, 5.52 per cent; C, 48.62 per cent; H, 5.94 per cent; N, 25.54 per cent, 25.60 per cent.

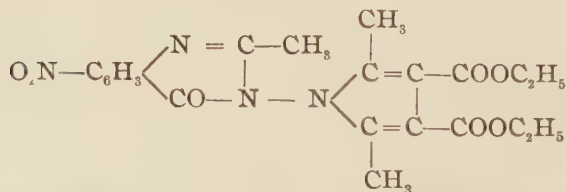
These figures do not correspond with those of either the phenylhydrazone of the phenylhydrazinoquinazolone, or of the osotetrazole derivative which would result from the former by loss of aniline.

II. The 3-aminoquinazolone was dissolved in alcohol, an excess of phenylhydrazine added and the solution made acid with acetic acid. It was then boiled for three hours under a reflux condenser. The unchanged aminoquinazolone was recovered.

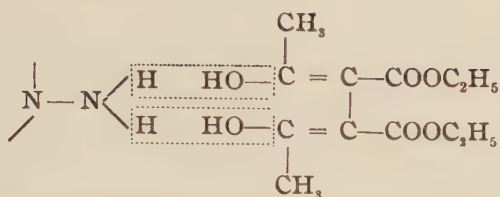
III. The aminoquinazolone was treated in nitrobenzol solution with two molecules of phenylhydrazine. Ammonia was evolved after short heating, but the product recovered from the reaction was the unchanged amino compound.

IV. The aminoquinazolone was treated in cumene solution with two molecules of phenylhydrazine. The heating was carried out under a reflux air condenser and continued for from five to six hours. Water and ammonia were liberated. On cooling, the reaction product crystallized; it was filtered and washed with ether, then dissolved and bone-blackened in alcohol and crystallized. The same product was obtained as by Method I. M. p. 230° (uncorr.).

7-Nitro-2-methyl-4-quinazolonyl-3-(2,5-dimethyl-3,4-dicarboethoxypyrrol).

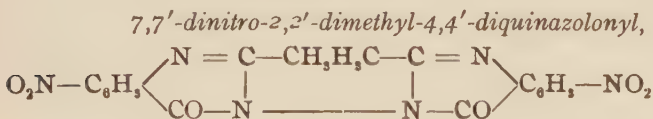


This compound is formed by the interaction between the 3-aminoquinazolone and diacetosuccinicediethyl ester, as shown below:



The 7-nitro-3-aminoquinazolone was boiled in glacial acetic acid solution with 25 per cent excess of diacetosuccinic diethyl ester for three hours. The acetic acid was then evaporated to very low bulk, and when cool, the unchanged aminoquinazolone caused to separate almost completely by scratching the sides of the beaker. This was filtered out and the mother liquor diluted with alcohol, causing the precipitation of a white compound. This, on recrystallization from alcohol, appeared in short white needles, melting sharply at 171°C . (corr.). The mother liquor remaining after the precipitation of this product contained a small amount of a yellow, granular compound, melting raggedly between 185° – 200°C ., which has not been identified.

Theoretical for $\text{C}_{21}\text{H}_{22}\text{N}_4\text{O}_7 = \text{C}$, 57.00 per cent; H, 4.97 per cent; N, 12.67 per cent. Found = C, 56.45 per cent; H, 4.8 per cent; N, 12.86 per cent.



In preparing the 3-aminoquinazolone, the 4-nitroacetantrhanil was always added to the hydrazine hydrate, in order to have an excess of the latter always present. In synthesizing the diquinazolonyl, the calculated amount of hydrazine hydrate was added to 4-nitroacetantrhanil, thus keeping the latter in excess and producing conditions much more favorable to a dimolecular condensation. The mixture was heated for a short time, and the cooled reaction mixture extracted with acetic acid (1:1). The residue was crystallized from a mixture of ethyl acetate and isoamyl acetate. The yield was poor. Small yellow granular crystals were obtained, melting at 337.5°C . (uncorr.). They are soluble in ethyl and isoamyl

acetates; also dissolved by acetic anhydride, with the production of a compound melting at 227°C . (uncorr.). This product was not investigated, but is probably an acetic anhydride addition product, such as was found by Bogert and Seil⁹ with the corresponding 5-nitro isomer.

N—Theoretical for $\text{C}_{18}\text{H}_{12}\text{N}_6\text{O}_6 = 20.58$ per cent. Found, 20.63 per cent.

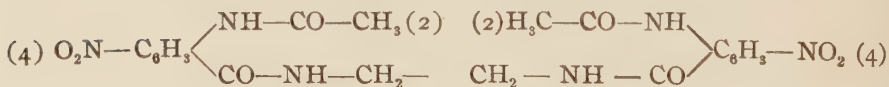
CONDENSATIONS WITH ETHYLENE DIAMINE.

The dimolecular condensation of ethylene diamine with 4-nitroacetanthranil yielded three different products by the following method: To 4-nitroacetanthranil was added the calculated quantity of ethylenediamine hydrate; the mixture was then heated on a sand bath till pasty, diluted with water and a small amount of alcohol, then filtered and extracted repeatedly with alcohol.

I. Reaction product insoluble in alcohol:

This was a very insoluble substance, showing no melting point; soluble only in nitrobenzol. The product obtained in this manner on the first trial was pale yellow. Analysis for N showed 17.77 per cent. The theoretical percentage for

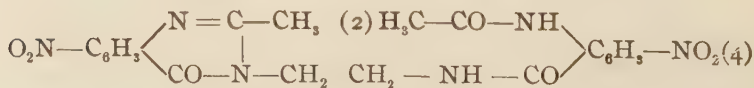
Di-(4-nitro-2-acetaminobenzoyl) Ethylenediamine,



$\text{C}_{20}\text{H}_{20}\text{N}_6\text{O}_8$ is 17.79 per cent.

In all subsequent condensations a yellow-green substance was obtained, soluble only in nitrobenzol and concentrated sulphuric acid. Analyses showed N 18.73 per cent, 18.54 per cent, 18.54 per cent. The theoretical percentage for the

4-Nitro-2-acetaminobenzoyl Derivative of 7-Nitro-2-methyl-3-ethylamine-4-quinazolone,

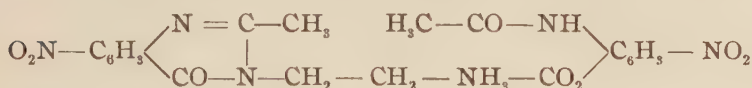


$C_{20}H_{18}N_6O_7$ is 18.50 per cent.

All attempts to condense this compound to the ethylenediquinazolonyl by means of dehydrating agents were unsuccessful. To this end the compound was boiled in acetic anhydride, phosphorus oxychloride and dissolved in cold concentrated sulphuric acid. In all cases the product was recovered unchanged, as shown by analysis.

II. Reaction product soluble in alcohol: ▀

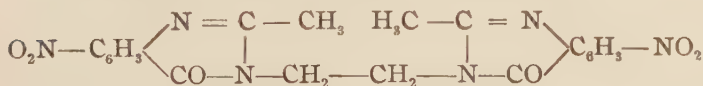
From the alcoholic extracts of the crude reaction product there was obtained by concentration a yellow crystalline substance, melting sharply at 258° C. (corr.) and resolidifying above that temperature. Only a small amount of this was obtained. N—Found—18.06 per cent. Its structure is probably isomeric with that of the substituted dibenzoylethylene-diamine. It may have the structure



Theoretical for $C_{20}H_{20}N_6O_8 = 17.79$ per cent.

A small amount of this compound was boiled with dilute caustic potash; it colored red. When analyzed for N it showed 19.17 per cent. The theoretical percentage for

Ethylenedi-(7-nitro-2-methyl-4-quinazolone),



$C_{20}H_{16}N_6O_6 = 19.26$ per cent N.

SUMMARY.

(1) 4-Nitroacetanthranil condenses readily with primary amines with the formation of 7-nitro-2-methyl-4-quinazolones.

(2) This reaction is applicable to all classes of primary amines with the exception of free amino acids and their salts.

(3) The acidic influence of the nitro group causes the 7-nitro-2-methyl-4-quinazalone to be soluble in alkaline carbonates and concentrated aqueous ammonia.

(4) The nitro group is reduced readily by stannous chloride to an amino group.

(5) Quinazolonyl acid amides are dehydrated by acetic anhydride with the formation of the corresponding nitriles.

(6) By the condensation of hydrazine with 4-nitroacet-anthranil, two products are obtained—the aminoquinazalone and the diquinazolonyl.

(7) The aminoquinazalone forms both mono- and diacetyl derivatives, each of which may be obtained from the other by suitable means.

(8) The keto group of the 7-nitro-2-methyl-4-quinazolones is very inactive. It is not affected by fusion with ammonium acetate and forms phenylhydrazones only on direct fusion with phenylhydrazine.

(9) The dimolecular condensation of ethylene diamine with 4-nitroacetanthranil proceeds only as far as one of the intermediate amide states.

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BIOGRAPHICAL.

William Klaber entered Columbia University in September, 1902, and graduated in June, 1905, receiving the degree of A.B. During the years 1905-'07 he pursued post-graduate work in the Department of Chemistry for the degree of Ph.D.

